GP1644

PATENT
7586/PD3033

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

SMITH et al.

Serial No: 08/392,934

Filed: 10/28/96

For: IMMUNOREACTIVE PEPTIDES FROM EPSTEIN-BARR VIRUS

Art Unit: 1644

Examiner: Ron Schwadron, Ph.D.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to:
Assistant Commissioner for Patents
Washington D.C. 20231, on
August 12, 1999
Date of Deposit
Wei-ning Yang
Name
08/12/99
Signature Date

RESPONSE TO RESTRICTION REQUIREMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

#3 Election
Goodhm
08/23/99

In response to the Restriction Requirement dated June 7, 1999, Applicant elects for prosecution the claims of Group I, claims 1, 31, 34 and 36 with traverse..

Claims 1 to 36 have been restricted to the following seven groups:

Group I Claims 1, 31, 34 and 36, corresponding to peptides and a kit containing said peptide;

Group II Claims 2-6, drawn to a method of detection using a peptide;

Group III Claims 7, 8, 32 and 35, drawn to antibodies, and a kit or composition containing said antibodies;

Group IV Claims 9-16, drawn to a method of detection using an antibody;

Group V Claim 17, drawn to a nucleic acid;

Group VI Claims 18-29, drawn to a method of therapy using an antibody; and

Group VII Claim 30, drawn to a method of therapy using a peptide.

The Examiner considered the peptides of the Group I invention as the putative technical feature linking Groups I-VII. The Examiner appears to believe that the peptides are obvious over Fox et al. in view of Pearson et al. for the reasons elaborated in the IPER (409 report) completed 2/21/95. Therefore, the Examiner restricts claims 1-36 into seven groups because of the belief that the technical feature linking the inventions of Groups I to VII does not constitute a special technical feature defined by PCT rule 13.2.

Applicants respectfully traverse the restriction requirements and respectfully submit that the peptides of Group I are not obvious in view of the references cited in the 409 report. Applicants submit that the peptides of Group I constitute a special technical feature that links claims 1-36 together, and therefore all the claims should be examined together in one application.

Claims 1, 31, 34 and 36 of Group I are not obvious over Fox et al. in view of Pearson et al. Claim 1 is directed to a polypeptide consisting essentially of an amino acid sequence selected from the group consisting of:

$[XETFTETWNRFITHTEY]_n$

$[XGMLEASEGLDGWIHQY]_n$

$[XHQQGGWSTLIEDNIPY]_n$

$[XKQKHPKKVKQAFNPLY]_n$

wherein X and Y are independently from 0 to 5 naturally occurring amino acids, wherein n is 1 to about 1000, wherein the polypeptide is capable of binding an antibody in a specimen from an individual with Epstein-Barr virus (EBV)-associated disease.

The first three peptides are polypeptides from the Epstein-Barr virus (EBV) early antigen-restricted (EA-R) 17 Kd, and the fourth peptide is a peptide from early antigen-diffuse (EA-D) 50 Kd regions. These polypeptides can be used for immunodiagnosis and immunotherapy of EBV-associated diseases.

Fox et al. have no teachings or suggestions that would have motivated one skilled in the art to arrive at the peptides of the present invention. Fox et al. have no teaching whatsoever of EA-R-derived peptides, much less of the first three peptides of claim 1, that are capable of binding an antibody in a specimen from an individual with Epstein-Barr virus (EBV)-associated disease. Instead, Fox et al. only teach that EA-D-derived immunogenic peptides have the capacity to immunologically bind antibodies induced by EA-D, and, therefore, can be effectively used for diagnosis of EBV-associated diseases. Fox et al. make no mention of any EA-R-derived peptides, let alone of their binding activities to antibodies from individuals with EBV-associated disease.

The teaching of the EA-D-derived peptides cannot make the EA-R-derived peptides of the present invention obvious. The binding activities of EA-D-derived peptides with EA-D-induced antibodies may not be used to predict the antibody-binding activities of EA-R-derived peptides from an EBV patient. The present invention has demonstrated the unpredictability of a peptide's binding acitivity with an antibody. In this regard, applicants would like to draw the Examiner's attention to Examples 2 and 4 of the present invention. According to the data summarized in Examples 2 and 4 of the application, the T-lymphocytes from EBV-infected individuals are recognized *only* by p17.1, the dominant epitope on p17 (see Example 2), whereas B-cells from EBV-infected individuals are recognized by three peptides from p17 (see Example 4), such as p17.1, p17.2 and p17.3. This data indicates that different peptides from the same region, i.e., p17, may have different antibody binding activities, let alone different peptides from different regions, i.e., from the EA-D or EA-R region. Because of the unpredictability of the antibody-binding activity of each peptide, One skilled in the art would not have reasonably predicted with certainty the immunoreactivities of the peptides of the present invention and therefore arrived at the peptides of the present invention in view of the teaching of Fox et al.

Fox et al. cannot make the fourth sequence of claim 1, the EA-D-derived synthetic peptide p50.10, obvious. First, Fox et al. have no teaching of the p50.10 peptide of claim 1. The p50.10 peptide of claim 1 has a different amino acid composition than the K5 polypeptide of Fox et al. In addition, the biological properties of the fourth peptide of claim 1 are different from those of K5. In this regard, applicants respectfully draw the Examiner's attention to Example 5 of the present invention on page 41 of the specification. In Example 5, the p50.10 peptide is

divided into portions A and B. Portion B of the p50.10 peptide is a region that overlaps with K5 of Fox et al. Example 5 shows that portion A has weak reactivity with IM sera, whereas portion B has no reactivity with IM sera. However, the intact p50.10 peptide shows unexpected good reactivity with IM sera (75% of the sera contained EA-D reactive antibody). Clearly, Example 5 of the present invention has demonstrated that the p50.10 peptide of the present invention provides unexpected immunoreactivity when compared to K5 of Fox et al. K5 of Fox et al. does not exhibit increased immunoreactivity with IM sera as compared to the normal sera (Fox et al., column 24, paragraph 1; Table 2). Since the p50.10 peptide provides unexpected results when compared to K5 of Fox et al., the p50.10 peptide of the present invention is not obvious in view of the teaching of Fox et al.

Pearson et al. cannot remedy the defect of Fox et al. Like Fox et al., Pearson et al. have no teaching whatsoever of the peptides of claim 1. Instead, Pearson et al. teach the entire amino acid sequence of the EBV EA-R 17 kDa protein. As admitted by the Examiner, the authors did not obtain EA-R peptides to improve immunoassay specificity for EA-R antibodies. In addition, based on the amino acid sequence of EA-R protein, one would not have reasonably predicated with certainty the EA-R-derived peptides of claim 1 for improved immunoassay specificities. As stated by Fox et al. [column 3, paragraph 1] "... even if a protein's amino acid residue sequence is known, methods for identifying the loci in the protein that constitute immunogenic and antigenic determinants are experimental in nature and *do not yield predictable results.*" Therefore, in view of the teachings of Fox et al. and Pearson et al., one would not have reasonably predicted with certainty the immunoreactivities of the peptides of the present invention and therefore arrived at the peptides of the present invention.

In conclusion, the cited references, either alone or in combination, would not have made the present invention as defined by claim 1, and its dependent claims 31, 34 and 36, obvious. Therefore, the peptides of the Group I claims constitute a novel, special, technical feature that links all the pending claims 1-36. Because this novel, special, technical feature makes a

contribution over the prior art, applicant respectfully requests the withdrawal of the restriction requirement to claims 1-36 of the present invention, and the examination of all the pending claims on the merits.

Respectfully submitted,

LOEB & LOEB LLP

Date: August 12, 1999

By: _____

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FORM PTO-1083

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SMITH et al.
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Wei-ning Yang
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Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Transmitted herewith is a Response to Restirction Requirement in the above-identified application.

☐ Small entity status of this application under 37 C.F.R. §§ 1.9 & 1.27 has been established by a verified statement previously submitted.

☐ A verified statement to establish small entity status under 37 C.F.R. §§ 1.9 & 1.27 is enclosed.

☐ A certified copy of ___ Patent Application No. ___ filed ___ from which priority is claimed under 35 U.S.C. § 119 is enclosed.

☒ No additional fee is required.

The fee has been calculated as shown below:

	(Col. 1) CLAIMS REMAINING AFTER AMENDMENT		(Col. 2) HIGHEST NUMBER PREVIOUSLY PAID FOR		(Col. 3) PRESENT EXTRA*	LG/SM $ ENTITY FEE		ADD'L FEE DUE
TOTAL CLAIMS FEE	36	-	36	**	0	LG=$18 SM=$9	$0	$ 0
INDEPENDENT CLAIMS FEE	1		3	***	0	LG=$78 SM=$39	$0	$ 0
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIMS						LARGE ENTITY FEE = $260 SMALL ENTITY FEE = $130		$ 0
							TOTAL	$ 0

* If the entry in Col. 1 is less than the entry in Col. 2, write "0" in Col. 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, write "20" in this space.
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, write "3" in this space. The "Highest Number Previously Paid For" (Total or Independent) is the highest number found from the equivalent box on Col. 1 of a prior amendment or the number of claims originally filed.

☐ A check in the amount of $___ to cover the additional claims fee is enclosed. **A copy of this sheet is enclosed.**

☐ A check in the amount of $___ to cover the extension fee is enclosed. **A copy of this sheet is enclosed.**

☒ The Commissioner is hereby authorized to charge any deficiencies of fees associated with this communication or credit any overpayment to Deposit Account No. 12-1820. **A copy of this sheet is enclosed.**

☒ Any filing fees under 37 C.F.R. § 1.16 for the presentation of extra claims
☒ Any patent application processing fees under 37 C.F.R. § 1.17

Respectfully submitted,
LOEB & LOEB LLP

Date: August 12, 1999

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